



PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: P. Coleman, et al.

Group Art No.: 1645

Serial No.: 09/821,877

Examiner: (not yet assigned)

Filed: March 30, 2001

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the:

Title: A HEPATITIS B VIRUS
SURFACE ANTIGEN MUTANT AND
METHODS OF DETECTION THEREOF

Commissioner for Patents
Washington, D.C. 20231, on:

Case No.: 6794.US.01

Date of Deposit: September 20, 2001

Tanya Benavidez 9/20/01
Tanya Benavidez Date

Commissioner for Patents
Washington D.C. 20231

Dear Sir:

SUBMISSION OF FORMAL DRAWINGS

Transmitted herewith are 7 sheets (FIG. 1 - FIG. 6) of corrected formal drawings as required in the Notice mailed on June 21, 2001, a copy of which is enclosed. Please replace the originally filed informal drawings with the formal drawings submitted herewith. If any problems exist with the enclosed Formal Drawings, the undersigned would appreciate a telephone call from the Draftsman as soon as possible.

Respectfully Submitted,
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Nucleotide sequence of the entire envelope gene for the mutant HBsAg strain:

ATGGGGCAGAATCTTTCCACCAGCAATCCTCTGGGATTCTTTCCCGACCACCAGTTGGAT
CCAGCCTTCAGAGCAAACACCAACAATCCAGATTGGGACTTCAATCCCAACAAGGACAC
CTGGCCAGACGCCAACAAGGTAGGAGCTGGAGCATTCTGGACTGGGGTTACCCCCACCGC
ACGGAGGCCTTTTGGGGTGGAGCCCTCAGGCTCAGGGCATAACACAAACCTTGCCAGCA
AATCCGCCTCCTGCTTCCACCAATCGCCAGTCAGGAAGGCAGCCTACCCCGCTGTCTCCA
CCTTTGAGAAACACTCATCCTCAAGCCATGCAGTGGAACCTCCACAACCTTCCACCAAACCT
CTGCAAGATCCCAGAGTGAGAGGTCTGTATTTCCCTGCTGGTGGCTCCAGTTCAGGAACAG
TAAACCCTGTTCCGACTACTGTCTCTCCCATATCGTCAATCTTCTCGAGGATTGGGGACC
CTGCGCGGAACATGGAGAACATCACATCAGGATTCCTAGGACCCCTGCTCGTGTTACAG
GCGGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTG
GACTTCTCTCAATTTTCTAGGGGGAACTACCGTGTGTCTTGGCCAAAATTCGCAGTCCC
CAACCTCCAATCACTCACCAACCTCCTGTCCTCCAACCTTGTCTGGTTATCGCTGGATGT
GTCTGCGGCGTTTTATCATCTTCTTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGT
TCTTCTGGACTATCAAGGTATGTTGCCGTTTGTCTCTAATTCCAGGATCTTCAACCAC
CAGCACGGGACCATGCAGAGCCTGCACGACTCCTGCTCAAGGAACCTCTATGTATCCCT
CCTGTTGCTGTACAAAACCTTCGGATGGAACTGCACCTGTATTCCCATCCCATCATCCT
GGGCTTTCGGAAAATTCCTATGGGAGTGGGCCTCAGCCCGTTTCTCCTGGCTCAGTTTAC
TAGTGCCATTTGTTCAGTGGTTCGTAGGGCTTTCCCCCACTGTTTGGCTTTCAGTTATATG
GATGATGTTGTACTGGGGGCCAAGTCTGTACACCATCTTGAGTCCCTTTTTACCGCTGTT
ACCAATTTTCTTTTGTCTTTGGGTATACATTAAACCCTAATAAA

FIG. 1

092187-09240

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Amino acid sequence of the entire envelope gene for the mutant HBV strain:

[preS1]MGQNLSTSNPLGFFPDHQLDPAFRANTNNPDWDFNPNKDTWPDANKVGAGAFGL
GFTPPHGGLLGWSPQAQGIQTLPANPPASTNRQSGRQPTPLSPPLRNTHPQA

[preS2]MQWNSTTFHQLQDPRVRGLYFPAGCSSSGTVNPVPTTVSPISSIFSRIGDPARN

[S]M₁ENITSGFLG₁₀PLLVLQAGFF₂₀LLTRILTIPQ₃₀SLDSWWTSLN₄₀FLGGTTVCLG₅₀QNSQS
PTSNH₆₀SPTSCPPTCP₇₀GYRWMCLRRF₈₀IIFLILLLC₉₀LIFLLVLLDY₁₀₀QGMLPVCPLI₁₁₀PGS
STTSTGP₁₂₀CRACTTPAAG₁₃₀TSMYPSCCCT₁₄₀KPSDGNCTCI₁₅₀PIPSSWAFGK₁₆₀FLWEWASA
RF₁₇₀SWLSLLVPFV₁₈₀QWFVGLSPTV₁₉₀WLSVIWMLY₂₀₀WGPSLYIILS₂₁₀PFLPLLPIFF₂₂₀CL
WVYI.

subtype ayw2, genotype D

Three S substitutions found:

- 1.) Thr to Ala 123 (affects H166 epitope)
- 2.) Trp to Leu 199 (outside "a" determinant)
- 3.) Ser to Thr 207 (outside "a" determinant)

FIG.2

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Nucleotide sequence of the small envelope gene for wild type HBV ayw₂:

ATGGAGAACATCACATCAGGATTCCTAGGACCCCTGCTCGTGTTACAGGCGGGGTTTT
TCTGGTTGACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGACTTCTCTC
AATTTTCTAGGGGGAACCTACCGTGTGTCTTGGCCAAAATTCGCAGTCCCCAACCTCCAA
TCACTCACCAACCTCCTGTCCTCCAACCTTGTCTGGTTATCGCTGGATGTGTCTGCGGC
GTTTTATCATCTTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTCTTCTGGA
CTATCAAGGTATGTTGCCGTTTGTCTCTAATTCCAGGATCATCAACCACCAGCACGG
GACCCTGCAGAACCTGCACGACTCCTGCTCAAGGAACCTCTATGTATCCCTCCTGTTGC
TGTACAAAACCTTCGGATGGAACTGCACCTGTATTCCCATCCCATCATCCTGGGCTTT
CGGAAAATTCCTATGGGAGTGGGCCTCAGCCCGTTTCTCTTGGCTCAGTTTACTAGTGC
CATTTGTTCAGTGGTTCGTAGGGCTTTCCCCACTGTTTGGCTTTCAGTTATATGGATGA
TGTGGTATTGGGGGCCAAGTCTGTACAGCATCTTGAGTCCCTTTTTACCGCTGTTACCA
ATTTTCTTTTGTCTTTGGGTATACATTTAA

FIG.3

Translated nucleotide sequence of the small envelope gene for the mutant HBV strain (1st sequence) and for wild type ayw₂ (third sequence). Differences in sequence are underlined.

S sequence-->

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GCG CGG AAC ATG GAG AAC ATC ACA TCA GGA TTC CTA GGA CCC CTG CTC GTG TTA CAG GCG
A R N M E N I T S G F L G P L L V L Q A
GCG CTG AAC ATG GAG AAC ATC ACA TCA GGA TTC CTA GGA CCC CTG CTC GTG TTA CAG GCG

GGG TTT TTC TTG ACA AGA ATC CTC ACA ATA CCG CAG AGT CTA GAC TCG TGG TGG ACT
G F L L T R I L T I P Q S L D S W W T
GGG TTT TTC TTG ACA AGA ATC CTC ACA ATA CCG CAG AGT CTA GAC TCG TGG TGG ACT

TCT CTC AAT TTT CTA GGG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC CCA ACC
S L N F L G G T T V C L G Q N S Q S P T
TCT CTC AAT TTT CTA GGG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC CCA ACC

TCC AAT CAC TCA CCA ACC TCC TGT CCT CCA ACT TGT CCT GGT TAT CGC TGG ATG TGT CTG
S N H S P T S C P P T C P G Y R W M C L
TCC AAT CAC TCA CCA ACC TCC TGT CCT CCA ACT TGT CCT GGT TAT CGC TGG ATG TGT CTG

CGG CGT TTT ATC ATC TTC CTC TTC ATC CTG CTG CTA TGC CTC ATC TTC TTG TTG GTT CTT
R R F I I F L F I L L L C L I F L L V L
CGG CGT TTT ATC ATC TTC CTC TTC ATC CTG CTG CTA TGC CTC ATC TTC TTG TTG GTT CTT

CTG GAC TAT CAA GGT ATG TTG CCC GTT TGT CCT CTA ATT CCA GGA TCI TCA ACC ACC AGC
L D Y Q G M L P V C P L I P G S S T T S
CTG GAC TAT CAA GGT ATG TTG CCC GTT TGT CCT CTA ATT CCA GGA TCA TCA ACC ACC AGC

ACG GGA CCA TGC AGA GCC TGC ACG ACT CCT GCT CAA GGA ACC TCT ATG TAT CCC TCC TGT
T G P C R A C T T P A Q G T S M Y P S C
ACG GGA CCC ACC TGC AGG ACC TGC ACG ACT CCT GCT CAA GGA ACC TCT ATG TAT CCC TCC TGT
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FIG.4A

TGC TGT ACA AAA CCT TCG GAT GGA AAC TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT
 C C T K P S D G N C T C I P I P S S W A
 TGC TGT ACA AAA CCT TCG GAT GGA AAC TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT

 TTC GGA AAA TTC CTA TGG GAG TGG GCC TCA GCC CGT TTC TCC TGG CTC AGT TTA CTA GTG
 F G K F L W E W A S A R F S W L S L L V
 TTC GGA AAA TTC CTA TGG GAG TGG GCC TCA GCC CGT TTC TCI TGG CTC AGT TTA CTA GTG

 CCA TTT GTT CAG TGG TTC GTA GGG CTT TCC CCC ACT GTT TGG CTT TCA GTT ATA TGG ATG
 P F V Q W F V G L S P T V W L S V I W M
 CCA TTT GTT CAG TGG TTC GTA GGG CTT TCC CCC ACT GTT TGG CTT TCA GTT ATA TGG ATG

 ATG TIG TAC TGG GGG CCA AGT CTG TAC ACC ATC TTG AGT CCC TTT TTA CCG CTG TTA CCA
 M L Y W G P S L Y I I L S P F L P L L P
 ATG TGG TAT TGG GGG CCA AGT CTG TAC AGC ATC TTG AGT CCC TTT TTA CCG CTG TTA CCA
 W S
 ATT TTC TTT TGT CTT TGG GTA TAC ATT TAA
 I F C L W V Y I
 ATT TTC TTT TGT CTT TGG GTA TAC ATT TAA

FIG.4B

Nucleotide sequence 492 to 675 encoding the "a" determinant for the mutant HBV strain.

T₄₉₂AT CAA GGT ATG TTG CCC GTT TGT CCT CTA ATT CCA GGA TCT TCA ACC ACC AGC
ACG GGA CCA TGC AGA G₅₆₁CC TGC ACG ACT CCT GCT CAA GGA ACC TCT ATG TAT CCC TCC TGT
TGC TGT ACA AAA CCT TCG GAT GGA AAC TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT
TTC GGA AAA₆₇₅

FIG.5

09021877 092401

Amino acid sequence of the "a" determinant for the mutant HBV strain:

Y₁₀₀QGMLPVCPLI₁₁₀PGSSTTSTGP₁₂₀CRACTTPAQC₁₃₀TSMYPSCCCT₁₄₀
KPSDGNCTCI₁₅₀PIPSSWAFGK₁₆₀

FIG.6